Radioprotection :

Is it really so important ?

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Société Française de Radiologie
Alger, le 27 avril 2019

Special thanks to :
Pr Hubert DUCOU LE POINTE

It is sometimes difficult to implement radiation protection

- Need for specific initial training and continuing education
- This represents a hardware cost (quality material regularly renewed)
- This represents a human cost (PCR, physician medical, REX…)
- This slows the flow of patients
- This can generate tensions with other doctors in the hospital
- Radiation protection is a complex area that can put off many even specialist operators
- Implementing a quality assurance approach is complex and requires ongoing efforts to maintain (Deming)
- …

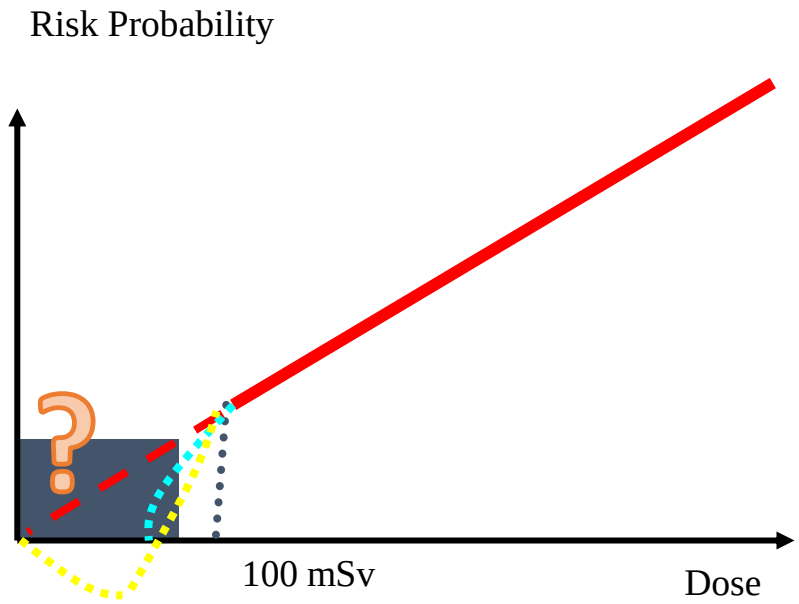
The biological effects of ionizing radiation

- Deterministic effects
  - Pertains to cutaneous, digestive, neurological effects, sterility
  - miscarriages, embryonic malformations, mental retardation
  - Can only occur above a threshold
  - This threshold can only be achieved for interventional radiology but is never achieved in conventional radiology or CT

  - => NO DETERMINISTIC EFFECTS

The biological effects of ionizing radiation

- Stochastic effects
  - Relates to transmissible genetic effects and carcinogenesis
  - Genetic effects have never been proven in humans, even after Nagasaki and Hiroshima
  - The increase in cancer risk is directly linked to the absorbed dose
    - But the regulation is based in greater part on the "Life-span study“
    - Nothing could really be proved below 200 mGy
    - There is uncertainty about the biological effects of low and very low doses
    - That is why the model of the linear relationship without threshold was invented



- => NO GENETIC EFFECTS
- => CANCER RISK FOR LOW DOSES = ?

- => NO DETERMINISTIC EFFECTS for conventional radiology and CT
- => NO GENETIC EFFECTS
- => CANCER RISK FOR LOW DOSES = ?

- => DIFFICULT AND EXPENSIVE TO IMPLEMENT

SO WHY ?

Deterministic effects to be considered in interventional radiology and for accidents

- In a normal use, the amount of radiation use doesn't lead to deterministic effects
- They are the result of improper use in diagnosis
- Scopy > 300 s or skin dose > 2 Gy are at risk => prevention and patients follow-up

The New York Times

Friday, October 16, 2009

Radiation Overdoses Point Up Dangers of CT Scans

2 ½-year-old, X-Ray technologist activated a CT scan 151 times on the same area.

"a clear line" on his face "consistent with the anatomical region that received the excessive radiation,"

Effets stochastiques

Mortality from breast cancer after irradiation during fluoroscopic examinations in patients being treated for tuberculosis.

• The mortality from breast cancer in a cohort of 31,710 women who had been treated for tuberculosis between 1930 and 1952

• 26.4 percent had received radiation doses to the breast of 10 cGy

• They had a relative risk of 4.5 per gray

•The data were most consistent with a linear dose-response relation.

•The risk was greatest among women who had been exposed to radiation when they were between 10 and 14 years of age

• The radiation effect appeared to peak approximately 25 to 34 years after the first exposure

Miller AB et al (1989)

N Engl J Med 321:1285–289

Cancer mortality among women frequently exposed to radiographic exams for spinal disorders

- Cohort of 5,573 women with scoliosis and other spine disorders diagnosed between 1912 and 1965. Median follow-up of 47 years

-The average (mean) age at scoliosis diagnosis in the analytic cohort was 10.6 years.

- A statistically significant elevated risk was observed only for breast cancer (SMR=1.68; 95% CI=1.38–2.02)

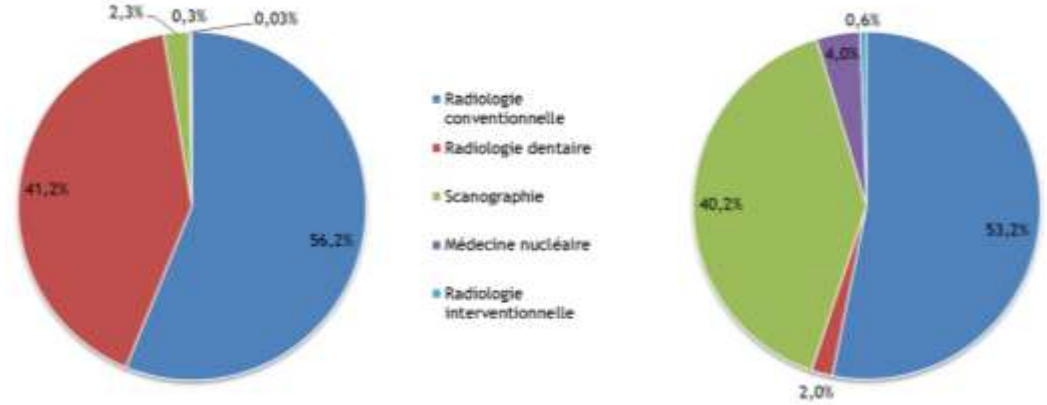
- The EAR (excess absolute risk) for breast cancer was 1.8 excess deaths per 10,000 woman-years of observation (95% CI: 1.0–2.6)

M. Ronckers (2010)

Radiat Res.174(1): 83–90

Contribution of CT to the total dose delivered

Frequency of medical procedures contribution to the total dose delivered



Adult population: CT scans accounted for 10.4% of the number of examinations and represented 71.3% of the total dose delivered

Pediatric population: CT scans accounted for only 2,3% of the number of examinations and represented 40.2% of the total dose delivered, Conventional radiology (56.2% of exams and 53.2% of the dose)

IRSN

Exposition de la population française aux rayonnements ionisants liée aux actes de diagnostic médical en 2012

Exposure of the French population to ionizing radiation related to medical, IRSN reports

IRSN

Exposition des enfants aux rayonnements ionisants due aux actes d'imagerie médicale diagnostique réalisés en France en 2015

Since 2001 (Brenner) cancer risk increases associated with CT scan have been suspected

Estimated Risks of Radiation-Induced Fatal Cancer from Pediatric CT

David J. Brenner[1]
Carl D. Elliston[1]
Eric J. Hall[1]
Walter E. Berdon[2]

OBJECTIVE. In light of the rapidly increasing frequency of pediatric CT examinations, the purpose of our study was to assess the lifetime cancer mortality risks attributable to radiation from pediatric CT.

MATERIALS AND METHODS. Organ doses as a function of age-at-diagnosis were estimated for common CT examinations, and estimated attributable lifetime cancer mortality risks (per unit dose) for different organ sites were applied. Standard models that assume a linear extrapolation of risks from intermediate to low doses were applied. On the basis of current standard practice, the same exposures (milliampere-seconds) were assumed, independent of age.

RESULTS. The larger doses and increased lifetime radiation risks in children produce a sharp increase, relative to adults, in estimated risk from CT. Estimated lifetime cancer mortality risks attributable to the radiation exposure from a CT in a 1-year-old are 0.18% (abdominal) and 0.07% (head)—an order of magnitude higher than for adults—although those figures still represent a small increase in cancer mortality over the natrual background rate. In the United States, of approximately 600,000 abdominal and head CT examinations annually performed in children under the age of 15 years, a rough estimate is that 500 of these individuals might ultimately die from cancer attributable to the CT radiation.

CONCLUSION. The best available risk estimates suggest that pediatric CT will result in significantly increased lifetime radiation risk over adult CT, both because of the increased dose per milliampere-second, and the increased lifetime risk per unit dose. Lower milliampere-second settings can be used for children without significant loss of information. Although the risk–benefit balance is still strongly tilted toward benefit, because the frequency of pediatric CT examinations is rapidly increasing, estimates that quantitative lifetime radiation risks for children undergoing CT are not negligible may stimulate more active reduction of CT exposure settings in pediatric patients.

- 600 000 CT head and abdomen < 15 yo
- 500 of these individuals might ultimately die from cancer attributable to the CT radiation
- Standard models that assume a <u>linear extrapolation of risks</u> from intermediate to low doses were applied.

AJR:176, February 2001

Since 2012, epidemiological studies of children and adolescents exposed to CT have been published

Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study

Mark S Pearce, Jane A Salotti, Mark P Little, Kieran McHugh, Choonsik Lee, Kwang Pyo Kim, Nicola L Howe, Cecile M Ronckers, Preetha Rajaraman, Sir Alan W Craft, Louise Parker, Amy Berrington de González

www.thelancet.com Published online June 7, 2012

- Cohort study 176,000 children exposed between 1985 and 2000
- Over 283,000 CT Median follow-up: less than 10 years

The risk is three times higher

Leukemia risk x 3.18. Red bone marrow dose ~50 mGy (5-10 head CTs)
Brain tumor risk x 2.82. Brain dose ~60 mGy (2-3 head CTs)
One excess case of brain cancer or leukemia per 10 000 CT scans of the head

Cancer risk in 680 000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians

John D Mathews *epidemiologist*[1], Anna V Forsythe *research officer*[1], Zoe Brady *medical physicist*[1 2],

- 680,000 children exposed to CT scan between 1985 and 2005
- 857,000 CT scans. Head: 59%, Facial bones: 13%, Extremities: 9,5%, Spine: 9%
- Mean follow-up: 9,5 years
- 3150 cases of cancer in the exposed group (680 211 people): 283 brain tumors, 643 cases of leukemia; 608 cases of cancer in excess
- Cancer incidence was 24% greater for exposed than for unexposed people
- The absolute excess cancer incidence rate was 9.38 per 100,000 person years at risk

BMJ 2013;346:f2360 doi: 10.1136/bmj.f2360 (Published 22 May 2013)

Risk of cancer incidence before the age of 15 years after exposure to ionising radiation from computed tomography: results from a German cohort study

L. Krille · S. Dreger · R. Schindel · T. Albrecht · M. Asmussen · J. Barkhausen · J. D. Berthold · A. Chavan · C. Claussen · M. Forsting · E. A. L. Gianicolo · K. Jablonka · A. Jahnen · M. Langer · M. Laniado · J. Lotz · H. J. Mentzel · A. Queißer-Wahrendorf · O. Rompel · I. Schlick · K. Schneider · M. Schumacher · M. Seidenbusch · C. Spix · B. Spors · G. Staatz · T. Vogl · J. Wagner · G. Weisser · H. Zeeb · M. Blettner

- The cohort included 71,073 CT examinations in 44,584 children

- For leukaemia,
The Standardised incidence ratios (SIR Observed/Expected) was 1.72

- For CNS tumours, the SIR was 1.35

Radiat Environ Biophys (2015) 54:1–12

Editorial J. Radiol. Prot. **34** (2014) E1–E5

Risks from CT scans—what do recent studies tell us?

Linda Walsh[1], Roy Shore[2], Anssi Auvinen[3], Thomas Jung[1] and Richard Wakeford[4]

- Dose reconstruction: Technical parameters retrieved from national surveys

- Absence of clinical information on the indication of the CT. Examinations could be performed because of suspected cancer (reverse causation) or diagnosis or monitoring of diseases themselves related to increased cancer risk (confounding bias).

-Pearce study included myelodysplastic syndrome (MDS) with leukemia cases . Without MDS cases risk was still high but not longer statiscally significant. (Unscear report)

The answer…

- There was evidence of some bias in our original risk estimates
- Information from the RIS and death certificates for about 40% of the cohort (n~180 000)
- Cancer-predisposing conditions in 4 out of 74 leukaemia/myelodysplastic syndrome (MDS) cases and 13 out of 135 brain tumour cases
- Evidence of previous unreported cancers in 2 leukaemia/MDS cases, 7 brain tumour cases and 232 in non-cases
- Exclusion of these cancers reduced the excess relative risk per mGy by 15% from for leukaemia/MDS and by 30% for brain tumours
- Re-analysis of the cohort with additional clinical data still showed an increased cancer risk after low-dose radiation exposure from CT scans in young patients

Berrington de Gonzalez A.,…, Pearce M.

Br J Cancer 2016 Feb 16;114(4):388-94

JNCI J Natl Cancer Inst (2019) 111(3): djy104

doi: 10.1093/jnci/djy104
Article

ARTICLE

Johanna M. Meulepas

Radiation Exposure From Pediatric CT Scans and Subsequent Cancer Risk in the Netherlands

- Retrospective cohort of 168 394 children who received one or more CT scans in a Dutch hospital between 1979 and 2012,
- The mean cumulative RBM (Red Bone Marrow) dose at the end of follow-up was 9.5 mGy and the mean brain dose was 38.5 mGy
- Statistically significant dose–effect relationship for brain tumors
- No association between the estimated cumulative RBM dose and incidence of leukemia.

- The EPI-CT study is coordinated by the International Agency for Research on Cancer (IARC).

- It was launched in 2011

- 9 national cohorts (Belgium, Denmark, France, Germany, Netherlands, Norway, Spain, Sweden and the United Kingdom **)**

- 1 million children expected to be included

- Pooled analysis concerning the estimations of the risks of cancer associated with CT scan exposure results should have been in the late 2015.
- No final results are currently published

Estimated size of cohorts

IJEA
International Journal of Epidemiology, 2018, 1–10
doi: 10.1093/ije/dyy231
Cohort Profile

Marie-Odile Bernier and al

Cohort Profile

Cohort Profile: the EPI-CT study: A European pooled epidemiological study to quantify the risk of radiation-induced cancer from paediatric CT

EPI-CT

- 1 430 454 CT scans was collected.
- The mean number of CT scans per patient was 1.5.
- The main areas examined were ‘head and neck’, ranging from 49.5% to 72.1% , followed by ‘chest’. Scans of multiple body parts represented 4.9% of the total number of CT scans.
- 4 national cohorts have published analyses of the relationship between CT exposure and cancer incidence.

IEA
International Journal of Epidemiology, 2018, 1–10
doi: 10.1093/ije/dyy231
Cohort Profile

Marie-Odile Bernier and al

Cohort Profile

Cohort Profile: the EPI-CT study: A European pooled epidemiological study to quantify the risk of radiation-induced cancer from paediatric CT

- Dose response relationship between CT-related dose and CNS tumours and leukaemia in exposed population (UK)
- German study reported a significantly increased incidence of cancer and lymphoma in exposed children compared with the general population.
- Dose related increase for leukaemia and CNS tumours (French), only for CNS tumours in German study
- The Dutch study reported a dose-response relationship for cranial CNS tumours and found no association with leukaemia

Hypersensitivity to radiation

- Progress (immunofluorescence) showing excess DNA damage at very low doses: 1-2 mGy
- Hypersensitivity to very low dose and low energy (cell survival curve)
- Cumulative effect and no splitting: 2 + 2 mGy worse than 4 mGy

Individual sensitivity

- Also available at low doses
- Proven ex-vivo on mammary epithelium
- In the conditions of mammography
- Depending on whether patients have low / high family risk (Colin 2011)

Radiological signature of cancers

- The lesions induced by ionizing radiation could be recognized (clusters)
- Demonstrated for thyroid cancer and sarcoma (Chevillard 2011)

100 Years of Individual Radiosensitivity: How We Have Forgotten the Evidence[1]

N, Foray et al :
Are *ATM*, *BRCA1*, *BRCA2*, and *P53* heterozygous carriers more susceptible to cancer eventually triggered by CT?

N Foray et al, Radiology 2012; 264:627–631

Representative Examples of Gene Mutations Unequally Associated with Radiosensitivity and Cancer Risk

Syndromes	Gene mutations	Incidence in the whole population	Radiosensitivity (SF2 in %)	Cancer risk
Ataxia telangiectasia	ATM−/−	1/40 000–1/300 000 (24)	1–3 (16,19,20,25)	5.8 for hematologic malignancies (26)
BRCA2 mutation (familial ovarian cancers)	BRCA2+/−	<1/800 (27)	10–40 (28)	>5 (eg, reference 29)*
BRCA1 mutation (familial breast cancers)	BRCA1+/−	1/500–1/800 (30)	30–50 (28)	>5 (eg, reference 31)*
Li-Fraumeni syndrome	P53+/−	<1/200 000 (32)	50–60 (28)	11.6 for rhabdomyosarcoma in carriers aged > 5 years (32)
Heterozygous ataxia telangiectasia	ATM+/−	0.36%–1% (33)	40–60 (16,19,20,25)	0–2.5 for breast cancer (33,34)

* Statistics on the cancer risk associated with *BRCA* mutations are still inconclusive, notably because of low statistical power of studies. Nevertheless, heterozygous *BRCA* carriers clearly show a significant risk of breast and ovarian cancer.

The ICRP considered that there is still not enough evidence to conclude that differences of radiosensitivity between individuals should be taken into account in the radiation protection system.

Health Protection Agency

Human Radiosensitivity

Report of the independent Advisory Group on Ionising Radiation

Documents of the Health Protection Agency

Radiation, Chemical and Environmental Hazards

March 2013

Individual sensitivity

- Known for high doses for a long time (radiotherapy)
- Discovered recently for small doses (lack of signaling alteration, therefore DNA repair)
- Would concern about 10% of the population

Exemple : 1% de la population est hétérozygote ATM

SYNDROMES GENETIQUES	GENE IMPLIQUE	ROLE DU GENE DANS LA REPARATION	SF2 (%)
Ataxie telangiectasie	ATM	Signalisation, contrôle NHEJ et MRE11	1-5
Syndrome Ligase IV	LIG4	NHEJ	2-6
Syndrome de Nimègue	NBS1	Voie MRE11	5-9
Progeria (Hutchinson-Gilford)	Lamin A	transport d'ATM	8-19
Ataxie telangiectasie (mutations homozygotes variantes)	ATM	Signalisation, contrôle NHEJ et MRE11	10-15
Syndrome d'Usher	Gènes USH	?	15-20
Syndrome de Cockayne	Gènes CS	Hélicases, nucléases NER	15-30
Xeroderma Pigmentosum	Gènes XP	Hélicases, nucléases NER	15-30
Syndrome ATLD	MRE11	Endonucléase, Voie MRE11	15-40?
Chorée de Huntington	IT15	?	18-30
Syndrome de Gardner	APC ?	MMR?	20-30
Syndrome de Turcot	hMSH2 ?	MMR?	20-30
Anémie de Fanconi et BRCA2	Gènes FANC	Protéine support	20-40
Syndrome BRCA1	BRCA1	Protéine support	20-40
Syndrome Artémis	Artémis	NHEJ	20-40
Syndrome Cernunnos	XLF/Cernunnos	NHEJ	20-40
Syndrome d'Omenn	RAG1, RAG2	NHEJ ?	30-50 ?
Syndrome Rothmund-Thomson	RecQ4	Hélicase	30-50
Syndrome de Werner	WRN	Hélicase	30-50
Syndrome de Bloom	BLM	Hélicase	30-50
Syndrome de Seckel	ATR	Signalisation	60-80
Témoins radiorésistants		60-80	60-80

% survie à 2 Gy

Why ?... Because…

- Deterministic risks are to be considered for interventional radiology and for accidents
- There is evidence of cell effects of very low doses in the laboratory
- Epidemiology : Increased risk for leukemia, brain tumors and lymphomas suspected by recent studies for CT scans during childhood – still waiting for large EPI-CT study results
- The sensitivity to ionizing radiation of some individuals can be very high !

Then…

- This justifies the utmost caution in the use of ionizing radiation
- Principle of justification (generic and individual)
- Optimization principle
- No dose limitation for patients but subject to good practice,
- do not forget dose limits for staff, the public, and the environment in some activities

Is it really so important ?

- So the answer is yes of course
- With implementation of the principles of radioprotection
- What goes through a quality assurance process
- Material choices
- Dose knowledge
- A formation of humans
- And especially excellent collaboration within teams and between teams and experience feedback
- That's why we are here together today

Merci beaucoup ! شكرا جزيلا ! Thank you very much !